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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,783	08/09/2005	Yuji Matsuzawa	10525.0014-00000	9334

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,783	MATSUZAWA ET AL.	
	Examiner	Art Unit	
	SAMUEL W. LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48 and 50-67* is/are pending in the application.

4a) Of the above claim(s) *2-44,46-48,50-54 and 56-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,45 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/13/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1-48 and 50-67 are pending.

Claim 49 was cancelled by the applicants' amendment filed 1/16/08. Claims 2-44, 46-48, 50-54, and 56-67 remain withdrawn. Claims 1, 45 and 55 and the elected SEQ ID NO:2 are examined in this Office action.

Restriction/Election

Applicants' response filed 8/13/08 argues that the process claims 66-67 are directed to the use of the protein recited in claims 1, 45 and 55 currently examined. According to applicant, the protein, composition, and kit of claims 1, 45, and 55 and the methods of claims 66-67 are not independent or distinct a search for the products and processes would be co-extensive and would not be burdensome upon the Examiner. Thus, the response requests co-examination of these claims1, 45, 55, 66 and 67 together (page 3 of the response). Applicants' argument that the products and processes are not independent or distinct is found unpersuasive because product claims 1, 45 and 55 are related to claims 66-67 as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the protein can be utilized in a materially different processes, e.g., producing an antibody that binds to the protein thereof. The search (I) for the protein (elected) and search (II) for a method of using said protein to modulate differentiation of

adipocyte claim 66) or/and to screen a compound capable of modulating the differentiation of adipocyte (claim 67) are not considered to be co-extensive. This is because lipid accumulation by a developing adipocyte which closely relates to adipocyte differentiation is a complex process that involves many changes in gene expression (p.1158, right col., Orlicky et al. (1998) *J. Lipid Res.*, 39, 1152-1161) that affects protein in vivo level; and thus, regulation of said differentiation or development the SEQ ID NO:2 protein requires extensive searches in addition to search for the protein structure *per se*. Thus, the requirements for searches I and II differ. Therefore, claims 66-67 and the elected invention of claims 1, 45 and 55 are patentably distinct from each other and are withdrawn from consideration as being drawn to a non-elected invention. Thus, the requirement is still deemed proper and is therefore made FINAL.

IDS

The references cited in the IDS filed 8/13/08 have been considered by Examiner.

Maintained-Claim Rejections 35 USC § 101 (lack of utility)

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1, 45 and 55 remain rejected under 35 USC 101 because the claimed invention is not supported by either a well-established or disclosed specific and substantial credible utility. For a utility to be "well-established" it must be specific, substantial and credible.

The protein of instant SEQ ID NO:2 is not supported by a specific asserted utility. The specification refers to the protein of SEQ ID NO:2 as "**SST20-14** (long form)" (see page 11, line

25) which is asserted to be a mouse white adipose tissue derived secretory protein (page 138, lines 15-18).

The specification asserts that the gene encoding "SST20-14" protein is specifically expressed in white fat tissue (page 56, lines 27-28).

The specification asserts that the "SST20-14" gene is decreased in expression at the time of fasting, and in response to stimulation of insulin resistance (page 56, lines 32-35), and further asserts that the excessive expression of said gene also suppresses differentiation of precursor adipocytes (page 37, lines 1-3).

The current invention is directed to the isolated protein comprising SEQ ID NO:2, i.e., "SST20-14". The above-asserted specific gene expression of "SST20-14" in white fat tissue is not considered to be a specific utility of the "SST20-14" protein. This is because regulation of an mRNA transcribing a protein is not considered to be an intrinsic property of the protein thereof. It is well known in the art that gene expression can be potently regulated through modulating the promoter which controls the gene expression or the mRNA transcription thereof. Thus, the results of specific "gene expression" may not reflect the function and usefulness *per se* of the protein which is the product of said gene expression. The art teaches that the expression of leptin, a protein produced in adipose tissue, is regulated by several extrinsic factors which are unrelated to the leptin structure and function (see page 768, left column, last two lines, Friedman et al. (1998) *Nature*, 395, 763-770).

The specification asserts that the "SST20-14" protein had a motif which can bind to lipid of lipoprotein (page 147, lines 13-14). Neither instant specification nor the art in the relative field provides factual indicia to show this amino acid sequence of motif and/or the binding of this

motif with other biological factors. The specification is completely silent in teaching the structural feature of this "motif" so as to compare it with motifs of proteins with known functions.

Many proteins or molecules can bind to lipid of a "lipoprotein", e.g., albumin which binds a wide variety of endogenous substances and drugs also is able to bind the fatty acid chain of acylated insulin (which here is considered to be a "lipoprotein") (see abstract, Kurtzhals et al. (1995) *Biochem. J.*, 312, 725-731). This indicates that binding to lipid moiety of a lipoprotein cannot be considered specific. Therefore, the above asserted utility of the "SST20-14" protein is a utility which would apply to every member of a general class of molecules, such as collection of proteins, but is only potential with respect to said protein. Because of this, such a utility is not specific and does not constitute a "well-established" utility.

The claimed protein of SEQ ID NO:2 is not supported by a substantial utility. The specification as filed does not disclose or provide any factual evidence that points to an activity having real world use (biological role or/and therapeutic role) of said polypeptide. The specification does not teach direct use of the claimed protein to treat a condition or disease or applied to a biological event having substantial utility. The specification contemplates that "SST20-14" gene expression is decreased in response to stimulation of insulin resistance (page 56, lines 32-35). However, the specification teaches nothing nor provides factual indicia as to whether "SST20-14" protein *per se*, but not DNA thereof, is applicable to treatment of insulin resistance. The art in the relative fields does not teach in this regard either. It is well-known in the art that the levels of mRNA do not necessarily correlate with the levels of the corresponding protein. See, *e.g.,* Chen et al. (*Mol. Cell Prot.* 1:304-313, 2002), which teaches "[t]he use of

mRNA expression patterns by themselves, however is insufficient for understanding the expression of protein products, as additional post-transcriptional mechanisms, including protein translation, post-translational modification, and degradation, may influence the level of a protein present in a given cell or tissue" (p. 304, right column). Furthermore, the specification does not disclose the core sequence(s) or domain(s) critical for biological function of "SST20-14". Hence, one skilled in the art is unable to compare "SST20-14" with known proteins that have real world utilities in order to practice the claimed invention.

The above-discussed asserted utilities constitute carrying out further research upon the protein being in hand to identify or reasonably confirm a "real world" context of use (e.g., diagnosing or/and treating a particular disease state). See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification must teach a skilled artisan how to use what is claimed and not merely provide a blueprint for further experimentation in order for an artisan to identify a use for the claimed invention. As stated in *Brenner v. Manson*, 383 U.S. 519 535-536,148 USPQ 689,696 (1966), "[a] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Thus, the test for substantial utility is not considered to be met; and therefore, the current application lacks substantial utility.

Claims 45 and 55 are directed to a composition and a kit comprising the protein of SEQ ID NO:2 or "SST20-14", respectively. Becasue the protein lacks specific and substantial utility discussed above, the composition of claim 45 and the kit of claim 55 also do not have a "well-established" utility.

The applicants' response to the 101 utility rejection

The response filed 8/13/08 submits (i) the claimed invention is directed to the isolated protein called i.e., "SST20-14" comprising SEQ ID NO:2, which has specific and substantial utility for influencing adipocyte development. The specification at pages 149-150 teaches that transfection of 3T3-L1 preadipocytes with an "SST20-14 (long form) expression construct (gene) reduces lipid drop accumulation as compared to no-transfected 3T3-L1 cells. Based on this "SST20-14" gene (DNA) transfection result, one skilled in the art could deliver the protein thereof to adipocytes to reduce proliferation of mature white adipocytes.

The applicants' argument is found unpersuasive because of the reasons below. The relative art (Orlicky et al. (1998) *J. Lipid Res*., 39, 1152-1161) teaches lipid accumulation by a developing adipocyte is a complex process that involves many changes in gene expression; where said "changes" result in storage of energy rather than its immediate use (p.1158, right col., last paragraph). This "lipid accumulation" relates directly to lipid metabolism in which many genes encoding proteins are involved (see p.47, right col. lines 1-12, Bernloher et al. (1999) *Semin. Cell Dev. Biol*., 10, 43-49). In the absence of sufficient teaching as to how the SEQ ID NO:2 protein involves in signal transduction pathway that regulates or reduce the "proliferation of mature white adipocytes adipocytes" asserted by applicants, the instant specification teaching at pages 149-150 is considered to be insufficient to establish the specific and substantial utility of said protein (note the instant claims are directed to the protein not DNA encoding the protein thereof). In the instant remarks, Applicant notes that "Transfection of 3T3-L1 preadipocytes with an SST20-14 (long form) expression construct…reduced lipid drop accumulation to 'half or less' as compared to non-transfected 3T3-L1 cells" (p. 4, bottom). Thus, it would appear that comparison is made between non-transfected cells and cells transfected with SST20-14

expression vector. There appears to be no negative control where a 3T3-L1 cell is transfected with the empty plasmid, pCMV-Tag4A, which is used for expression of the SST20-14 gene (see page 149, lines 17-18). The relative art (Scott et al. (2002) *J. Biol. Chem.*, 277, 27693-37701) teaches that transfection of HEK-293 cells with empty control plasmid "pCMV-Tag4A" (p. 37695, column 1, top) results in ~ 50% decrease of calcium signal (p. 37700, left col., 2nd paragraph, lines 16-18), suggesting that the empty expression vector pCMV-Tag4A *per se* is capable of reducing cellular calcium signaling, which, in turn, would appear to inhibit or reduce lipid accumulation; this is becasue $[Ca^{2+}]_i$ (intracellular calcium) stimulates triglyceride (precursor of lipid) accumulation and lipogenesis (see p.80, left col., lines 20-3, Shi et al. (2000) *Physiol. Genomics*, 3, 75-82), i.e., decrease of the $[Ca^{2+}]_i$ would inhibit/reduce the lipogenesis or lipid accumulation. Since the instant specification lacks this critical control (use of "pCMV-Tag4A" transfected cell rather than the cell alone), the effect of "*reducing lipid drop accumulation as compared to no-transfected 3T3-L1 cells*" asserted by response above does not necessarily reflect the activity of "SST20-14" protein of SEQ ID NO:2 but rather is the result of transfecting the cells with pCMV-Tag4A vector, which is the vector for constructing the SST20-14 expression construct. Thus, pages 149-150 of the specification do not provide sufficient factual indicia to support the applicants' submission "one skilled in the art could deliver the protein thereof to adipocytes to reduce proliferation of mature white adipocytes". As such, further experimentation is required to determine whether or not the protein of SEQ ID NO:2 has the alleged activity of "reduced lipid drop accumulation". Therefore, the claimed protein of SEQ ID NO:2 lacks the asserted substantial utility.

Also, the response asserts that, as the specification at page 1 teaches that the SST20-14 protein provides an attractive avenue toward treating such diseases by impeding the underlying fat accumulation, such the asserted pharmaceutical use would satisfies the utility requirement. Thus, the response requests withdrawal of the 101 utility rejection.

This argument is unpersuasive because the asserted pharmaceutical use of the SST20-14 protein at page 1 of the specification is hypothetical and lacks factual evidence/support from the instant specification as well as the relative art as noted above. Thus, the claimed protein is not supported by a substantial utility. In view of the discussions above, the claimed protein (claim 1), the composition (claim 45) and the kit (claim 55) comprising said protein do not have the well-established utility nor the asserted specific and substantial utility. Thus, the rejection stands.

Maintained-Claim Rejections - 35 USC § 112, the first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement rejection

Claims 1, 45 and 55 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

This rejection stands for the reasons set forth in the foregoing statement of the grounds of rejection under 35 U.S.C. 101.

The specification fails to teach that the disclosed protein comprising instant "SST20-14" of SEQ ID NO:2 has useful biological activity which relates to the above-discussed specific and substantial utility for the reasons of record and those set forth above. Accordingly, the protein (claim 1), the composition (claim 45) and the kit (claim 55) comprising the protein thereof have no therapeutic or biological applications. Thus, one skilled in the art is unable to use the claimed protein, or/and the composition comprising the protein for modulating differentiation of adipocytes, or/and the kit comprising the protein for screening a compound which has specific affinity for the protein thereof.

The applicants' response to the enablement rejection

At page 5, the response filed 8/13/08 asserts that as the "SST20-14" protein is useful for inhibiting adipocyte maturation, i.e., has specific and substantial utility, one skilled in the art would not require undue experimentation to use the claimed invention; and thus, request withdrawal of the rejection.

The applicants' argument is found unpersuasive because of the reasons of record and those set forth above with regard to the lack of specific and substantial utility of the claimed "SST20-14" protein, and because one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. Thus, the rejection is deemed proper and maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

/Samuel W Liu/
Examiner, Art Unit 1656
November 3, 2008

/David J. Steadman/
Primary Examiner, Art Unit 1656